Occupational Risk Factors for Breast Cancer Among Women in Shanghai

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Although female breast cancer rates are lower in China than in Western countries, rates have been rising rapidly in China. This increase may be due to changes in established breast cancer risk factors, but it is possible that exposure to occupational and environmental carcinogens in Shanghai also have contributed to the rise in incidence. We used data collected by the Shanghai Cancer Registry and the Chinese Third National Census to study the risk of breast cancer by occupation and by occupational exposures. Standardized incidence ratios (SIRs) were used to compare observed cases to expected numbers of cases, based on the incidence rates for Shanghai and the number of women in each occupation according to the 1982 census. Statistically elevated SIRs for breast cancer were seen for a number of professional occupational categories, with the greatest risk seen among scientific research workers (SIR = 3.3). Administrative clerks, political and security personnel, and makers of rubber and plastics products also had significant excesses. Significant deficits of risk were seen for the categories of production and related workers, construction workers, and transportation equipment operators. For specific occupations, the highest SIRs were observed among doctors of Chinese-Western medicine (SIR = 14.7, 95% CI = 5.9–30.3) and doctors of Chinese medicine (SIR = 7.2, 95% CI = 4.4–11.4). We also found excesses among teachers at each level of education, librarians, clerical workers, electrical and electronic engineers, nurses, lab technicians, accountants and bookkeepers, rubber manufacturing products makers, weavers, and knitters. SIRs were significantly elevated for high probability of exposure to organic solvents (SIR = 1.4). For benzene exposure, we found significant excesses for overall exposure (SIR = 1.1) and for medium level of exposure (SIR = 1.3). There was no evidence of an association between risk and electromagnetic fields (EMF) exposure. Based on a small number of exposed, SIRs were elevated for both medium probability and high level of exposure to pesticides. The elevations in occupations reported here support some previous reports. Our finding of an increased risk associated with benzene also has been reported previously; the finding for organic solvents is new. However, the literature on the risk of breast cancer related to occupational exposures is limited and there is no consistent body of literature for any of the exposures studied here. Further, many comparisons were made and the problem of multiple hypothesis testing cannot be ignored in a survey such as ours. Am. J. Ind. Med. 34:477–483, 1998. © 1998 Wiley-Liss, Inc.†

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INTRODUCTION

Chinese women have lower rates of breast cancer than Western women, but the rates among Chinese women are rapidly rising [Dai, 1995]. While changes in risk factors such as increased age at first birth, decrease in parity, and dietary changes may explain some of the increase in incidence, it is

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possible that increased exposure to occupational and environmental carcinogens in industrialized Shanghai also have contributed to the rise in incidence. Results of occupational studies conducted in Western countries thus far have been inconclusive. Exposures such as organic solvents [Labrèche and Goldberg, 1997], pesticides [Davis et al., 1993], electromagnetic fields [Loomis et al., 1994; Stevens and Davis, 1996] as either environmental or occupational exposures have been proposed as possible risk factors for breast cancer, but have not been widely studied as workplace exposures. The results of studies of breast cancer risk and pesticide levels measured in either serum or adipose tissue have been conflicting [Welp et al., 1998], as have been those of studies of EMFs and breast cancer [Loomis et al., 1994; Cantor et al., 1995a; Goldberg and Labrèche, 1996]. We used data collected by the Shanghai Cancer Registry and the Chinese Third National Census to study the risk of breast cancer by occupation and occupational exposures among women in Shanghai, China.

METHODS

Methods used for this cancer occupation linkage study have been published previously [Chow et al., 1993; Gao et al., 1993]. Briefly, occupational information was collected for all incident cancer cases aged 30 years or older diagnosed from the years 1980 through 1984 in urban Shanghai. Information on occupation at the time of diagnosis or retirement for those who had retired before diagnosis was obtained from the patient or next of kin for 98.3% of cases. These data were compared to the 1982 census data (National Bureau of Statistics, China) for the same population. Occupations were categorized and coded according to the standardized coding scheme used in the 1982 census (National Bureau of Statistics, China). With this coding scheme, occupations were categorized into broad categories (onedigit codes), specific categories (two-digit codes), and were given individual codes (three-digit).

Age-adjusted standardized incidence ratios (SIRs) for female breast cancer were computed by occupational categories, specific occupations, and by occupational exposures. We selected exposures based on a possible link with breast cancer risk suggested in previous epidemiologic and experimental studies. These exposures included organic solvents, benzene, electromagnetic fields, and pesticides. Job exposure matrices for these substances were developed by the industrial hygienist for this project (M.D.) based on previous experience in industrial settings in China and elsewhere. Each occupation was given a score for the probability (none, low, medium, high) and level (none, low, medium, high) of exposure. For each agent, SIRs were computed for each probability, each level, probability by level, and across all probabilities and levels (ever exposed).

RESULTS

SIRs were elevated for breast cancer in the occupational categories (Table I) of scientific research worker (SIR = 3.3, 95% CI = 1.4–6.5), medical and public health workers (SIR = 1.5, 95% CI = 1.3–1.8), economists and financial planners (SIR = 1.4, 95% = 1.2–1.7), teachers (SIR = 2.0, 95% CI = 1.8–2.2), administrative clerks (SIR = 1.6, 95% = 1.3–1.9), political and security personnel (SIR = 2.1, 95% = 1.6–2.6), and rubber and plastics products makers (SIR = 1.8, 95% = 1.4–2.3). Deficits of risk were seen for the categories of other production and related workers (SIR = 0.6, 95% CI = 0.5–0.8), construction workers (SIR = 0.5, 95% CI = 0.3–0.9), and transportation equipment operators (SIR = 0.3, 95% CI = 0.2–0.6).

The greatest excesses seen for specific occupations (Table II) were among doctors of Chinese-Western medicine (SIR = 14.7, 95% CI = 5.9–30.3), doctors of Chinese medicine (SIR = 7.2, 95% CI = 4.4–11.4), university and higher education teachers (SIR = 2.6, 95% CI = 1.7–3.7), middle school and technical teachers (SIR = 2.4, 95% CI = 2.0–3.0), kindergarten instructors (SIR = 2.7, 95% CI = 1.5–3.4), and librarians (SIR = 2.3, 95% CI = 1.2–4.0). Excesses were also found for electrical and electronic engineers, nurses, lab technicians, accountants and bookkeepers, rubber manufacturing products makers, knitters, and weavers. In contrast, waiters, other production workers, dockers and freight handlers, and warehouse workers had low SIRs.

In Table III we present SIRs by probability and level of selected exposures, and across all probabilities and levels of exposure (overall exposure). There was no excess risk related to overall exposure to organic solvents. SIRs were elevated for high probability (SIR = 1.4, 95% CI = 1.1-1.8) and high level of exposure (SIR = 1.1, 95% CI = 0.9-1.2), but there was no clear pattern of increasing risk with probability or level of exposure. No excess risk was seen for overall exposure to benzene. A high probability of exposure to benzene was related to a 30% increase in risk (SIR = 1.3, 95% CI = 1.0-1.7). For level of exposure, both medium and high levels had elevated SIRs. There were no significant associations with probability or level of exposure to EMFs. Overall exposure to pesticides was not related to risk of breast cancer. Based on small numbers, the SIR was elevated for medium probability of exposure and for high level of exposure.

The SIRs for analyses of probability by level of exposure are presented in Table IV. The highest elevation in risk for solvent exposure was among women with high probability and high level of exposure. Increases of risk with benzene exposure were driven by the combination of medium and high probabilities and levels of exposure. The results for pesticides were unstable due to small numbers, but an elevated risk was seen among women with a high probability and level of exposure. This group had an SIR of

TABLE I. Standardized Incidence Ratios for Breast Cancer by Occupational Category, Shanghai, 1980–1984^a

Code	Occupational Category	Observed	SIR	95% CI
0-1/0-2	Scientific research workers	8	3.3	1.4-6.5
0-3/0-4	Industrial technician	47	1.0	0.7-1.3
0-5	Administrators in science and technology	13	1.4	0.7-2.4
0-7/0-8	Medical and public health workers	134	1.5	1.3-1.8
0-9	Economists and financial planners	141	1.4	1.2-1.7
1-1	Teachers	266	2.0	1.8-2.2
1-4	Cultural workers	20	1.6	1.0-2.5
2-2	Leaders of parties and mass organizations	27	1.3	0.9-2.0
2-3	Leaders of administrative units in towns and villages	19	1.4	0.8-2.2
2-4	Leaders of business organizations	55	1.3	1.0-1.7
3-1	Administrative clerks	103	1.6	1.3-1.9
3-2	Political and security personnel	69	2.1	1.6-2.6
3-3	Postmen and communication workers	15	1.4	0.8-2.4
4-1	Salesmen, shop assistants and related workers	130	1.1	0.9-1.3
4-2	Purchasing agents, suppliers and marketing staff	18	1.5	0.7-3.0
5-1/5-2	Public service workers	290	1.0	0.8-1.1
5-3	Cooks	54	0.6	0.4-1.8
5-5	Home appliance repair	54	0.6	0.6-1.9
7-2	Metal refining and processing	33	0.8	0.6-1.2
7-3	Chemical processors and related workers	22	1.0	0.6-1.5
7-4	Rubber and plastics products makers	60	1.8	1.4-2.3
7-5	Textile workers (spinners, weavers, knitters, dyers and related workers)	396	1.1	1.0-1.2
7-7	Tailors	106	0.9	0.7–1.1
7-6	Leather and fur processors	19	1.0	0.6-1.5
7-9	Tobacco preparers and tobacco product makers	6	0.5	0.2-1.1
8-2	Printers and related workers	22	0.9	0.6-1.4
8-5	Machinery fitters, machine assemblers and precision instrument makers (except electrical)	144	1.0	0.8–1.1
8-6	Electrical fitters and related electrical and electronics workers	102	0.9	0.8–1.1
8-8	Plumbers, welders, sheet metal and structural metal preparers and erectors	36	0.8	0.6–1.2
9-0	Painters	17	0.9	0.5–1.4
9-1	Other production and related workers	37	0.6	0.5-0.8
9-2	Construction workers	11	0.5	0.3-0.9
9-4	Materials handling and related equipment operators, dockers and freight handlers	32	0.7	0.5–1.0
9-5	Transportation and equipment operators	10	0.3	0.2-0.6
9-9	Other transportation and production workers	107	0.9	0.8–1.1

aSubcategories with more than five cases were included. SIR, standard incidence ratio; 95% CI, 95% confidence interval.

1.3, but confidence intervals included unity. There were no significant findings for exposure to EMFs.

DISCUSSION

We found statistically significant excesses of breast cancer among women whose usual occupation was in professional occupational categories, including scientific research workers, medical and public health workers, economists and financial planners, teachers, and leaders of business organizations. When we explored the risk of breast cancer by specific occupations, we found elevations among electrical and electronic engineers, doctors of Chinese

medicine, doctors of Chinese-Western medicine, nurses, accountants and bookkeepers, teachers of each level of education, and librarians. Elevated risks of breast cancer among professional women have been observed previously in registry-based studies [Goldberg and Labrèche, 1996]. However, in two recent case control studies of breast cancer in which occupational histories were obtained, women with a history of employment in the professional occupational category were not at increased risk [Coogan et al., 1996; Petralia et al., 1998]. Women with specific occupational titles of teacher and nurse did not have an increased risk of breast cancer in either study. In other studies, nurses [Roman et al., 1985; Rubin et al., 1985; Gunnarsdottir and Rafnsson,

TABLE II. Age-Adjusted Standardized Incidence Rates for Breast Cancer by Occupation, Shanghai, 1980–1984^a

Code	Occupation	Observed	SIR	95% CI
0-33	Electrical and electronic engineers	18	1.8	1.1–2.8
0-34	Mechanical engineers and technicians	7	0.7	0.3-1.3
0-35	Chemical engineers and technicians	9	1.1	0.6-1.8
0-52	Assistant administrators for science and technology	13	1.4	0.8-2.5
0-71	Doctor of Chinese medicine	19	7.2	4.4-11.4
0-72	Doctor of Western medicine	23	0.8	0.5-1.2
0-73	Doctor of Chinese-Western medicine	7	1.5	5.9-30.3
0-74	Pharmacists and assistants	6	1.4	0.5-2.9
0-75	Nurse	53	1.9	1.4-2.5
0-76	Lab technicians	11	2.0	1.0-3.6
0-77	Public health workers	14	1.4	0.8-2.3
0-92	Statisticians	23	1.3	0.8-2.0
0-93	Accountants and bookkeepers	104	1.6	1.4-2.0
0-97	Bankers	9	2.2	1.0-4.1
1-11	University and higher education teachers	27	2.6	1.7-3.8
1-12	Middle school and technical teachers	103	2.4	2.0-3.0
1-13	Primary education teachers	107	1.8	1.5-2.2
1-14	Kindergarten Instructors	24	2.3	1.5-3.4
1-45	Librarian	12	2.3	1.2-4.0
2-21	Leaders of parties	17	1.2	0.7-1.9
2-22	Leaders of the youth league, trade unions, and women's associations	10	1.7	0.8-3.2
2-32	Leaders of resident committees	19	1.4	0.9-2.3
2-41	Managers of business organizations and factories	22	1.7	1.1-2.6
3-21	Political instructors	6	0.7	0.3-1.5
3-32	Telephone and telegraph operators	10	1.3	0.6-4.3
4-11	Salesmen, shop attendants, and demonstrators	125	1.1	0.9-1.3
4-21	Purchasing agents	8	1.5	0.7-3.0
4-22	Sales personnel and suppliers	10	1.2	0.6-2.2
5-11	Waiters	20	0.6	0.4-0.9
5-12	Hotel and restaurant personnel	11	1.4	0.7-2.5
5-17	Babysitters and childcare workers	41	1.0	0.7-1.3
5-18	Housekeepers	9	0.6	0.3-1.1
5-22	Sanitation personnel, street cleaners and garbage men	10	0.7	0.3-1.3
5-23	Miscellaneous workers (doormen, messengers, janitors)	171	1.1	0.7-0.9
5-29	Other public service workers	13	1.1	0.6-1.9
6-11	Grain farmers	7	1.2	0.5-2.5
7-38	Pharmaceutical manufacturing workers	12	1.6	0.8-2.7

1995; Bulbulyan et al., 1992; Cantor et al., 1993; Morton, 1995] and teachers [Doebbert et al., 1988; Bulbulyan et al., 1992; King et al., 1994; Morton, 1995] have been reported to be at increased risk of breast cancer. Our finding of excesses among accountants, bookkeepers, and librarians are consistent with previous studies [Goldberg and Labrèche, 1996].

Our results suggested that rubber manufacturing makers may have an excess of breast cancer. Exposures in this industry include solvents, particularly benzene. However, no excess mortality from breast cancer was found in two cohort studies of rubber workers [Monson and Nakano, 1976;

Delzell and Monson, 1981; Solionova and Smulevich, 1993].

We found some indication of an increased risk of breast cancer among women exposed to organic solvents, specifically benzene. The biological plausibility of a link between breast cancer and organic solvents, including benzene, has been discussed in detail [Labrèche and Goldberg, 1997]. Some individual solvents such as benzene, 1–2-dibromoethane, 1–1- and 1–2-dichloroethane, and vinyl chloride are mammary carcinogens in animals. In humans, the terminal duct lobular units exhibit high proliferative activity and

TABLE II. Age-Adjusted Standardized Incidence Rates for Breast Cancer by Occupation, Shanghai, 1980–1984^a (continued)

Code	Occupation	Observed	SIR	95% CI
7-41	Rubber manufacturing and product makers	22	1.8	1.1–2.8
7-42	Plastic manufacturing and product makers	35	1.3	0.9-1.8
7-52	Spinners and winders	119	1.0	0.8-1.2
7-53	Textile machinery mechanics	8	0.9	0.4-1.8
7-54	Weavers	166	1.2	1.0-1.4
7-55	Knitters	69	1.3	1.0-1.6
7-56	Bleachers, dyers, and textile product finishers	22	1.3	0.8-2.0
7-59	Other textile workers	7	0.4	0.1-0.7
7-62	Leather products workers	19	1.1	0.7-1.8
7-72	Tailors and sewers	75	1.0	0.7-1.2
8-12	Paper product makers	43	0.9	0.7-1.3
8-23	Printing pressmen	8	1.0	0.4-1.9
8-24	Bookbinders	10	0.9	0.4-1.6
8-42	Toolmakers, metal pattern makers, and metal workers	11	8.0	0.4-1.5
8-44	Metal grinders, polishers, tool sharpeners, and machine-tool operators	74	1.1	0.9-1.4
8-49	Other blacksmiths, toolmakers, and machine tool operators	37	0.9	0.6-1.9
8-51	Machinery fitters and machine assemblers	13	1.1	0.6-1.8
8-52	Machinery, motor vehicle, and aircraft engine mechanics	13	1.4	0.8-1.2
8-53	Watch, clock, and precision instrument makers	12	0.7	0.4-1.3
8-63	Electric and electronic equipment	59	0.9	0.7-1.2
8-64	Electricians (electrical wiremen), other electric linemen, and cable jointers	10	1.0	0.5-1.9
8-82	Welders and flame cutters	18	1.4	0.8-2.1
8-83	Sheet metal workers	18	0.7	0.4-1.1
8-91	Glass workers (formers, cutters, grinders, finishers, and engravers)	15	1.4	0.8-2.4
9-19	Other production and related workers	25	0.6	0.4-0.9
9-41	Dockers and freight handlers	18	0.6	0.3-0.9
9-94	Warehouse workers	34	0.7	0.5-0.9

^aOccupations with 5 or more cases were included; 95% SIR, standard incidence ratio; 95% CI, 95% confidence intervals.

susceptibility to chemical carcinogens and are therefore considered likely target tissues for carcinogenesis [Telang et al., 1990].

Our findings for benzene are similar to those of a case-control study of breast cancer in which occupational histories were linked to a job exposure matrix for benzene exposure (Petralia et al. submitted). In this study, risk increased with probability, but not with intensity of exposure. Our results are also in agreement with results of a cohort study of leather tanners exposed to benzene in which women had an excess of breast cancer deaths [Mikoczy et al., 1994]. Our results are not in agreement with those of a large cohort of workers exposed to benzene in China in which no excess of breast cancer deaths were detected [Yin et al., 1996]. However, the women in the cohort were young (60% of person-years were contributed by women who were under 30 years of age at study entry) and only 2% of the cohort were deceased at the time those results were reported. Nevertheless, that study had a superior study design and exposure assessment compared to our study, and so the

findings raise some concern regarding the validity of the findings presented here. Additionally, a cohort study of shoe manufacturers exposed to benzene were not at increased risk of dying of breast cancer [Paci et al., 1989].

Occupational exposure to organic solvents in general were not found to be related to breast cancer mortality in a registry-based study [Cantor et al., 1995b]. Women exposed to solvents in general in a cohort of aircraft maintenance workers had an elevated breast cancer mortality rate compared to female cohort members with no solvent exposure [Blair et al., 1998]. Elevated breast cancer risk has been reported for certain other individual solvents. In two cohort studies [Blair et al., 1998; Shannon et al., 1988] and in one registry study [Cantor et al., 1995a, 1995b], excesses of breast cancer were found among women with occupational exposure to methylene chloride. Nonsignificant increases in the risk of dying of breast cancer was seen for workers exposed to polyvinyl chloride [Chiazze et al., 1977, 1990]. There is little epidemiologic evidence of an association for other individual solvents, such as trichlorethylene. In a

TABLE III. Standardized Incidence Ratios for Breast Cancer by Probability and Level of Exposure, Shanghai, 1980–1984^a

Probability Level **Exposure** SIR 95% CI N SIR 95% CI Organic solvents 0 0 P_1 727 1.0 0.9 - 1.1 L_1 615 1.0 0.9 - 1.1 P_2 77 144 0.9 0.7 - 1.0 L_2 8.0 0.8 - 1.1 P_3 73 1.4 1.1 - 1.8 L_3 222 1.1 0.9 - 1.2All 1,828 1.0 0.9 - 1.1Benzene 0 P_1 16 1.0 0.9 0.6 - 1.30.5 - 1.6L 31 P_2 77 1.0 0.8 - 1.6 L_2 60 1.3 1.0 - 1.7 P_3 50 1.3 1.0 - 1.7 L_3 5 1.3 1.0 - 1.7ΑII 250 1.1 1.0 - 1.4Pesticides 0 P_1 0.5 0.8 0.4 - 1.56 0.2 - 1.1 L_1 10 4 P_2 6.5 1.8 - 1.7 L_2 0 9 9 P₂ 1.3 0.6 - 2.5 L_3 1.3 0.6 - 2.5ΑII 69 1.0 0.6 - 1.50 **FMF** 0 P_1 683 0.9 - 1.11.0 0.9 - 1.0602 1.0 P_2 72 1.1 0.9 - 1.40 L_2 P_3 72 0.9 0.7 - 1.2 L_3 130 1.0 0.8 - 1.2All 827 0.9 - 1.01.0

aSIR, standarized incidence ratio; 95% CI, 95% confidence intervals.

cohort study, women exposed to trichlorethylene in an aircraft maintenance facility were found to have no elevated risk of death due to breast cancer [Spirtas et al., 1991]. A more recent follow-up of this cohort revealed that compared to nonexposed female cohort members, women exposed to trichlorethylene had a nonsignificant excess of breast cancer deaths, but no excess of breast cancer morbidity [Blair et al., 1998]. Women employed in dry cleaning, an occupation involving exposure to trichlorethylene, have not been found to be at an increased risk of breast cancer [Blair et al., 1979, 1990; Ruder et al., 1994].

EMF was not related to breast cancer in this study. Although studies have shown that EMF can suppress the production of melatonin, a hormone that has been shown to protect against breast cancer [Stevens and Davis, 1996], the epidemiologic evidence for a link between risk of breast cancer and occupational exposure EMF has been weak and inconsistent [Goldberg and Labrèche, 1996]. The data on occupational exposure to pesticides and risk of breast cancer are sparse. No elevations in the risk of breast cancer were detected in a study of gardeners [Hansen et al., 1991] or

TABLE IV. Standardized Incidence Ratios for Breast Cancer, Probability by Level of Exposure, Shanghai 1980–1984^a

	Probability				
Laurel	1	2			
Level	n SIR 95% CI	2	3		
Benzene					
1	16, 1.0, 0.5–1.6	18, 0.8, 0.5-1.3	0, —		
2	3, 0.7, 0.1–2.0	57, 1.4, 1.1–1.8	0, —		
3	0, —	2, 2.0	50, 1.0, 2.0–1.7		
Solvent					
1	605, 1.0, 0.9-1.1	10, 1.4, 0.7–2.5	0, —		
2	49, 0.7, 0.5-1.0	28, 1.1, 0.7-1.6	0, —		
3	73, 1.2, 0.9–1.5	76, 0.8, 0.7–1.1	73, 1.4, 1.1–1.8		
Pesticides					
1	6, 0.5, 0.2-1.1	4, 6.5, 1.8–1.7	0, —		
2	0, —	0, —	0, —		
3	0, —	0, —	9, 1.3, 0.6–2.5		
EMF					
1	588, 1.0, 0.9-1.1	14, 0.9, 0.5-1.6	0, —		
2	61, 0.8, 0.6–1.0	0, —	0, —		
3	34, 0.7, 0.5-0.9	58, 1.2, 0.9-1.5	92, 0.7-1.2		

^aSIR. standardized incidence ratio: 95% CI, 95% confidence intervals.

among women with a high probability of occupational exposure to insecticides [Cantor et al., 1995b].

Limitations of this study must be considered. Data on other possible confounding factors, particularly reproductive factors, were not available. Some of these factors, such as age at first birth, may have been related to occupation. Our finding of an increased risk among professionals may be confounded by reproductive history or by other factors related to socioeconomic status. An additional potential weakness of the study is that only one job was used to classify workers. However, there was relatively little job mobility in China in the early 1980s, and the one-time occupational information used in our study was a reasonable representation of usual occupation [Dosemeci et al., 1996]. It should be noted that, due to a high rate of growth in China during the past decade, occupational exposures and breast cancer risk may have changed since the period of the study. Therefore, the results presented here may not represent current occupational risk factors for breast cancer in China. The problem of multiple comparisons is also a concern in a survey such as ours of numerous occupational categories.

In conclusion, the results from this record linkage study in Shanghai showed elevated risk of breast cancer among women in several professional occupations, among rubber workers, women exposed to organic solvents in general, and women exposed to benzene. However, our findings should be considered exploratory or hypothesis generating. Further research into the possible link between breast cancer risk

and exposure to both benzene and organic solvents is warranted. Studying organic solvents in general may mask true relationships between particular solvents and breast cancer risk, as only certain solvents are mammary carcinogens in rats, and/or have been shown to be associated with an increased risk in epidemiologic studies. Therefore, we suggest that organic solvents be studied individually rather than as a group.

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